LONG-TERM NON-INTERVENTIONAL SAFETY STUDY OF EMICIZUMAB TREATMENT IN PATIENTS WITH MODERATE HAEMOPHILIA A AND SEVERE BLEEDING PHENOTYPE (STUDY BO44691, PASS)

First published: 13/06/2024

Last updated: 12/05/2025

Study Planned

Administrative details

EU PAS number

EUPAS1000000174

Study ID

1000000174

DARWIN EU® study

No

Study countries

- ☐ Canada
- ☐ France

☐ United Kingdom

☐ United States

Study description

This non-interventional (NI) post-authorization safety study (PASS) is a multi-country, registry-based, longitudinal cohort study based on secondary use of data collected from multiple registries. It includes patients of all ages with moderate congenital Haemophilia A (Factor VIII [FVIII] 1%-5%), without FVIII inhibitors and with severe bleeding phenotype, treated with emicizumab. The aim of the study is to evaluate the long-term safety profile of emicizumab in these patients who are exposed to emicizumab in real-world settings, with a specific focus on thromboembolic (TE) events.

Study status

Planned

Research institutions and networks

Institutions

IQVIA

☐ United Kingdom

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Last updated: 22/04/2024

Institution | **Non-Pharmaceutical company** | **ENCePP partner**

Contact details

Study institution contact

Letizia Polito letizia.polito@roche.com

Study contact

letizia.polito@roche.com

Primary lead investigator

Letizia Polito

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 20/10/2024

Actual: 01/01/2023

Study start date

Planned: 01/05/2026

Data analysis start date

Planned: 31/12/2030

Date of final study report

Planned: 30/06/2031

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

F. Hoffmann-La Roche, Ltd.

Study protocol

Prot BO44691 emicizumab v2, Published Output-1_Redacted.pdf (1.97 MB)

Prot BO44691 emicizumab v3, Published Output_Redacted.pdf (1.8 MB)

Regulatory

Was the study required by a regulatory body?

Yes

Is the study required by a Risk Management Plan (RMP)?

EU RMP category 3 (required)

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

This non-interventional (NI) PASS is a multi-country, registry-based, longitudinal cohort study based on secondary use of data collected for patients of all ages with moderate congenital Haemophilia A, without FVIII inhibitors and with severe bleeding phenotype, treated with emicizumab.

Main study objective:

The aim of the study is to evaluate the long-term safety profile of emicizumab in patients with moderate congenital Haemophilia A (FVIII 1%-5%) without FVIII inhibitors and with severe bleeding phenotype and who are exposed to emicizumab in real-world settings, with a specific focus on thromboembolic (TE) events.
The primary objective for this study is to determine the incidence of TE events.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine

HEMLIBRA

Study drug International non-proprietary name (INN) or common name

EMICIZUMAB

Anatomical Therapeutic Chemical (ATC) code

(B02BX06) emicizumab

emicizumab

Medical condition to be studied

Haemophilia A without inhibitors

Population studied

Short description of the study population

Patients of all ages with moderate congenital Haemophilia A, without FVIII inhibitors and with severe bleeding phenotype, treated with emicizumab

Age groups

All

Paediatric Population (< 18 years)

Neonate

Preterm newborn infants (0 – 27 days)

Term newborn infants (0 – 27 days)

Infants and toddlers (28 days – 23 months)

Children (2 to < 12 years)

Adolescents (12 to < 18 years)

Adult and elderly population (≥18 years)

Adults (18 to < 65 years)

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Elderly (≥ 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Estimated number of subjects

200

Study design details

Setting

Inclusion criteria:

• Diagnosis of congenital Haemophilia A (HA);

• Moderate disease classification (FVIII 1%-5%);

• Severe bleeding phenotype prior to initiation of emicizumab;

The above-mentioned inclusion criteria will ensure that the patient is eligible for the extended indication of emicizumab.

In addition, the patient will have to fulfil the following criteria:

• Initiation of emicizumab treatment during the cohort entry period;

• Continuous enrolment in the registry for 12 months prior to initiation of emicizumab (i.e., with one healthcare visit, diagnosis, laboratory test, treatment, or self-reported information recorded in the registry at least 12 months before initiation of emicizumab);

• Signed the informed consent form where required by local regulations.

Exclusion criteria:

• Noted development of FVIII inhibitors any time prior to initiation of emicizumab or fulfilling any of the criteria of a previously developed algorithm (Batt et al., 2022).

• Treatment with emicizumab at any time prior to the Marketing Authorization for the expanded indication in the respective country.

Outcomes

The primary objective for this study is to determine the incidence of TE events.

The secondary objectives for this study are:

1. To determine the incidence of serious adverse events (SAEs).
2. To determine the incidence of thrombotic microangiopathy (TMA) events.
3. To determine the incidence of serious systemic hypersensitivity reactions, including anaphylaxis.
4. To characterise the risk profile in terms of pre-defined risk factors of TE events in the patient population.
5. To describe characteristics of TE events, SAEs, TMA events, and serious systemic hypersensitivity reactions, including anaphylaxis (e.g., diagnosis and symptoms).
6. To characterise the impact of the prior use of FVIII prophylaxis on the incidence of TE events, SAEs, TMA events, and serious systemic hypersensitivity reactions, including anaphylaxis.

Data analysis plan

This study does not include any formal comparison and is purely descriptive.

For the primary objective and secondary objectives 1, 2, and 3, the overall crude and crude stratified incidence rates (IRs) will be calculated. The person-time of each patient will be based on the follow-up and censoring criteria.

For the calculation of crude IRs, the denominator will be the pooled person-time of all the patients within the cohort. The patient time-at-risk will be calculated

from the index date until the date of an incident event or censoring, whichever occurs first.
All first events occurring during the follow-up period will be counted in the total number of events. Crude IRs will be presented per 100 person-years (PY) with 95% CI.
For the primary objective, the numerator will be the number of first TE events of all patients within the cohort. For secondary objectives 1, 2, and 3, the numerators will be the number of first occurrences of any SAE, TMA events, or serious systemic hypersensitivity reaction events, respectively.
For secondary objective 4, calculation of crude stratified IRs of 1st TE events will be done. The events will be counted for each category/stratum of relevant pre-defined risk factors of TE events. In addition, for all recorded TE events, pooled patient characteristics will be presented by tabulating their demographic, clinical, and co-morbidity variables.
For analysis of secondary objective 5, subtypes/details and characteristics of TE events, SAEs, TMA events, and serious systemic hypersensitivity reactions (e.g., diagnosis and symptoms), will be tabulated. In addition, time to the 1st TE, SAE, TMA events, and serious systemic hypersensitivity reactions will be described by Kaplan-Meier curves.
For analysis of secondary objective 6, calculation of crude IR and crude incidence proportion of TE, TMA events, SAEs, and serious systemic hypersensitivity reactions, will be calculated and tabulated for FVIII prophylaxis use (yes/no) prior to emicizumab

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data source(s)

FranceCoag

Data source(s), other

UK National Haemophilia Database (UKNHD), American Thrombosis and Hemostasis Network (ATHN) dataset, and Canadian Bleeding Disorders Registry (CBDR)

Data sources (types)

Disease registry

Use of a Common Data Model (CDM)

CDM mapping

Yes

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

Unknown